3cd4_: K-----KVVLGKKGDTVELTCTASQKKS----IQFHWK—
NSNQIKILGNQGSFLTKGPSKLNDRAD-SRRSL

2rhe_:
ESVLTQPPSASGTPGQRVTISCTGSATDIGSNSVIWYQQVPGKAPKLLIYY---
NDLLPSGVSDRFSAS----

3cd4_: WDQGNFPLIIKNLK----
IEDSDTYICEVEDQKEEVQLLVFGLTANSDTHLLQGQSLTLTLESPPGSSPSV
QC

2rhe_: KSGTSASLAISGLESEDEADYY---CAAWNDSLDEPG----------
FGGGTKLTVLGQPK------

3cd4_:
RSPRGKNIQGGKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIVVLA

2rhe_: ----------

5fd1_: AFVVTDNCIKCKYTDCVEVCPVDCFYEGPNFLVIHPDEC-
IDCALCEPECP-AQAIFSEDEVPEDM-QEFIQL

2fxd_: ----------PKYTIVDKETCI-----
ACGACGAAAPDIYDYDEDGIAYVTLDDN

5fd1_: NAE----LAEVWPNITE-KKDPLPDAEDWDGVKGKLQHLER---

2fxd_: QGIVEVP-DILIDDMMDA--FEGCPTDSIKVADEPFDGDPNKFE

Compilation of the modeling results

Due to its stochastic character, the entire simulation procedure was repeated several times for each case of the target template chains. The resulting structures were then subject to a refinement run. Namely, the algorithm employed in the first stage of the Monte Carlo modeling (starting from the initial, "old" threading-based alignment and performing all the updates of the alignment described in the "implementation of the template restraints" section) was used in short isothermal runs at low (T=1) temperature, with the final structure obtained at the end of the first

state of Monte Carlo used as input. At this temperature, the model did not change any of its global features, rather only local fluctuations were seen. The average conformational energy, which included the intrinsic force field of the model and the effect of template restraints, was then used to select the "best" structure. The model had quite a strong RMSD versus energy correlation far from the native state. Closer to native state, the two quantities became uncorrected or the correlation was weak, depending on the case. It should be pointed that out that this refers to the entire force field (intrinsic and the template biases). A quite different situation was observed for just the intrinsic force field; this was the strongest correlation of RMSD versus energy near the native structure (unpublished results). Since all the models were, at best, of moderate resolution, this criterion was no better than the one based on the total energy. The lowest average (total) energy conformation from these short isothermal runs was selected for further consideration. For example, in the case of ltlk, a structure that had a RMSD of 4.4 Å from native was selected, while several simulations resulted in structures about 3 Å from native.

Tables X and XI, below, contain a compilation of the simulation results.

Table X. Alpha carbon RMSD from native for models built from the initial threading alignments and refined by lattice simulations.

Target Protein	Threading +MODELLER	SICHO +MODELLER
1aba_	4.43	4.86
1bbhA	6.77	6.82
1cewI	14.96	14.38
1hom_	7.82	3.70
1stfI	6.40	5.95
1tlk_	7.23	4.17
256bA	6.09	4.36
2azaA	21.95	10.77
2pcy_	6.56	4.41
2sarA	10.28	7.83
3cd4_	6.74	6.39
5fd1_	25.67	12.40

Note: The threading + MODELLER models use the threading alignments (for the aligned residues) as the target for all-atom reconstruction. SICHO models are the reduced lattice models obtained by the method described in this work. The final all-atom model is also built by MODELLER using as a target the lattice model alpha carbon positions estimated from the SICHO lattice model. The values of the RMSD for alpha-carbon traces (in Å) are given for the structured parts of the target molecules (1hom_: residues 7-59, ltlk_: residues 9-103, 3cd4_: residues 1-97 *i.e.*, the first domain).

Table XI. Alpha carbon RMSD (in Å) from native for models built by MODELLER and by lattice simulations SICHO for the aligned residues only.

Target Protein	Starting RMSD	MODELLER RMSD	SICHO RMSD	Length
1aba_	4.37	3.89	4.40	69
1bbhA	7.03	6.35	6.69	116
1cewI	12.88	12.37	10.74	69
1hom_	5.59	5.34	3.45	40
1stfI	7.05	6.04	4.73	83
1tlk_	7.88	7.15	3.94	86
256bA	6.92	6.06	4.37	104
2azaA	11.04	13.53	9.94	80
2pcy_	7.64	6.65	4.36	94
2sarA	8.28	8.07	7.60	73
3cd4_	5.72	5.56	5.22	82
5fd1_	12.38	12.18	11.94	69

Note: The starting RMSD is for the set of threading-aligned residues of the template from the equivalent native target coordinates. The MODELLER models use the threading alignments and an all-atom target. SICHO models are the all-atom models built by MODELLER using the lattice models (only Cα) as a target. The length of the alignments is given in the last column.

In Table X, the Cα RMSD from the native are compared for two kinds of molecular models. The first were generated using the initial threading template followed by automated modeling using MODELLER. While this homology modeling tool is not intended to be used in such a way, some means was needed for